

of chest-pain within 72 hours, or ongoing chest-pain, were included. ECG criteria to be fulfilled was transient or persisting ST-depression and/or T-wave inversion. Subcutaneous injections of dalteparin 120 IU/kg were given twice daily the first 6 days followed by 7500 IU once daily the following 35-45 days. P-fibrinogen (Fib.) and P-CRP were measured at inclusion. Event rates (%) during the 150 days follow-up period were evaluated in relation to median levels of fibrinogen and CRP.

**Conclusion:** In patients with unstable coronary artery disease initially treated with dalteparin, and long term treatment with aspirin, elevation of fibrinogen and CRP at admission indicates an increased risk of subsequent acute myocardial infarction and death. The importance of inflammation as a pathological component in unstable coronary artery syndromes needs further evaluation.

2:30

### 793-3 C-Reactive Protein in Unstable Angina: Lack of Association With Ischemic Activity or Complex Lesion Morphology

Deven J. Patel, Charles J. Knight, Nicolas A. Chronos, Colin Salisbury, Debbie Clarke, Christine Wright, Alison H. Goodall<sup>1</sup>, Kim Fox. *Royal Brompton Hospital, London, UK; <sup>1</sup> Royal Free Hospital, London, UK*

C-reactive protein (CRP), a sensitive marker of inflammation, is elevated in unstable angina (UA) although it is not known whether a high CRP relates to ischemic activity or complex lesion morphology (CLM). CRP levels were measured, (Beckman turbidimetric method), in 72 pts (53 males), mean age 63.6 (46-79) yrs, with refractory UA (Braunwald class IIIB). Transient myocardial ischemia (TMI) was detected using continuous ST segment monitoring and angiographic analysis was performed by two observers blinded to other study data. Median CRP was 0.89 mg/dl (0.48-20.75), and was elevated (> 1 mg/dl) in 32 (44%) pts. TMI was present in 20 (28%) pts despite maximal medical therapy. 14 (19%) pts had 1 vessel disease, 22 (31%) 2 vessel, and 36 (50%) 3 vessel disease. CLM was present in 35 (49%) pts and thrombus in 7 (10%). Pts with TMI had similar CRP levels and was raised in a similar proportion (see table). Pts with CLM had similar CRP levels, although CRP was higher in pts with multi-vessel disease ( $P < 0.05$ ). CRP was raised in 4/7 (57%) pts with thrombus.

CRP > 1 mg/dl (%)	TMI 8 (40%)	No TMI 24 (46%)	CLM 15 (43%)	No CLM 27 (46%)	1 VD 4 (29%)	2 VD 7 (32%)	3 VD 21 (58%)
Median	0.8	0.95	0.74	0.99	0.69	0.88	1.12
(range)	0.5-21	0.5-7.9	0.5-21	0.5-7.9	0.5-7.9	0.5-21	0.5-20

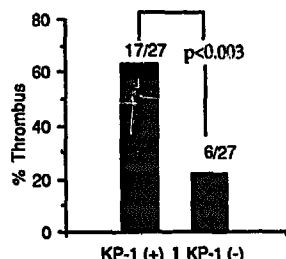
**Conclusion** Although CRP is elevated in refractory unstable angina, and is associated with multi-vessel disease, it does not predict ischemic activity or angiographic markers of acute plaque rupture.

2:45

### 793-4 Inflammation & Thrombosis in Unstable Angina. Insights From Directional Coronary Atherectomy Tissue Analyses

Samin K. Sharma, Billie S. Fyfe, Ram Bongu, Jonathan D. Marmur, Srinivas Duvvuri, Thomas P. Cocke, John A. Ambrose. *Mount Sinai Hospital, NY*

Plaque disruption with thrombus (T) is the major pathogenetic mechanism for the acute coronary syndromes of myocardial infarction and unstable angina (UA). Recently, clinical studies have suggested a role for inflammation in UA. The relationship between inflammation and thrombus in UA has not been well studied. Analysis of tissue from directional atherectomy specimens can be used to correlate inflammation and thrombus. Thus, we analyzed the results of immunohistochemical staining for macrophages (KP-1) in 54 culprit lesions (19 with rest angina, 15 with new onset/crescendo, 10 post-infarction and 10 with stable angina). Thrombus was detected by H and E staining. KP-1



staining was graded as 0 to 2+ and 2+ was considered positive(+). Pathologic specimens were analyzed blindly.

Thrombus was found predominantly in rest angina and post-infarction. KP-1 staining was more common in all syndromes other than stable. A positive KP-1 was significantly associated with thrombus particularly in rest angina and post-infarction where 14 of 17 KP-1 positive lesions were positive for thrombus. Thus, these data suggest a strong association between inflammation and thrombus in unstable rest angina and post-infarction.

3:00

### 793-5 Measurement of Leukocyte Sequestration and Adhesion Molecule Expression in the Coronary Circulation of Unstable Angina Patients

Roberto R. Giraldez, Carlos V. Serrano, Beth Noble, Pamela Ouyang, David Bush, Roy Ziegelstein, Jay L. Zweier. *The Johns Hopkins Medical Institutions, Baltimore, MD*

Polymorphonuclear leukocyte, PMN, adhesion and activation has been demonstrated to be of great importance in the mechanisms of myocardial ischemia and reperfusion injury. Evidence from animal models demonstrates that upon activation by inflammatory mediators, PMNs are trapped in the coronary circulation. Despite the important role of PMNs in posts ischemic injury, little is known concerning the accumulation of these cells in the heart after interaction with unstable plaques. This study evaluated the magnitude of PMN sequestration in the coronary circulation of unstable angina (UA) patients and the changes in the expression of adhesion molecules caused by interaction with active lesions. Ten UA patients undergoing catheterization within the first 48 hours of symptoms and four control patients (Ct) had blood samples collected simultaneously from the aorta (Ao) and coronary sinus (CS) prior to the injection of contrast medium. PMN counts revealed a small but significant decrease in the number of cells collected in the CS compared to the Ao ( $p < 0.05$ ). PMNs also had typical L-selectin (activation associated) shedding ( $p = 0.001$ ). This pattern of activation, however, was not paralleled by CD11b and CD18 adhesion molecules, suggesting that cells which had this integrin upregulation remained sequestered due to adhesion to the coronary endothelium.

Group	Coronary Sinus Cell Count	L-selectin	CD11b	CD18
UA (n = 10)	0.93 ± 0.03*	0.79 ± 0.05**	1.04 ± 0.12	0.88 ± 0.1
Ct (n = 4)	0.99 ± 0.03	1.04 ± 0.01	1.00 ± 0.05	0.98 ± 0.03

Results expressed as % of control (Ao measurements); \* $p < 0.05$ , \*\* $p = 0.001$

Thus, in unstable angina L-selectin shedding and PMN accumulation occurs within the coronary circulation which may in turn contribute to further vascular or myocardial damage.

3:15

### 793-6 Plasminogen Activation in Unstable Angina Is Associated With an Acute Phase Response but Not With Activation of the Hemostatic System

Luigi M. Biasucci, Giovanna Liuzzo, Gaetano Quaranta, Laura Massa, Giuseppina Caligiuri, Claudia Monaco, Francesco Summaria, Willy van de Greef, Antonio G. Rebuzzi, Cornelis Kluft<sup>1</sup>, Attilio Maseri. *Cardiology Institute, UCSC-Rome, Italy; <sup>1</sup> PG-TNO Gaubius Inst. Leiden, NL*

Coronary thrombosis is the major pathogenetic event leading to ischemia in pts with unstable angina (UA). This event involves the coagulation and the fibrinolytic systems, and, possibly, the inflammatory system. To assess the role of activation of fibrinolytic system and its relation with the hemostatic and the inflammatory systems, we measured plasma levels of Plasmin- $\alpha$ 2-antiplasmin (PAP), C-Reactive protein (CRP) and Thrombin-AntiThrombin III (TAT), as markers of plasminogen activation, inflammation and thrombin production, respectively. We also measured plasma levels of D-Dimer (DD), a fibrin degradation product, to assess actual lysis of fibrin. We studied 32 pts admitted to our CCU for severe UA. Blood samples were taken at CCU admission. As controls (C) we studied 20 healthy volunteers. **Results** (median and range): Elevated levels were considered above mean  $\pm$  2 SD for PAP (700 ng/ml), DD (70  $\mu$ g/l) and TAT (4  $\mu$ g/ml) and levels  $> 3$  mg/l for CRP (90<sup>th</sup> percentile of healthy subjects). Elevated levels of PAP were observed in 16/32 pts (50%), but elevated levels of DD and TAT were found only in 5/32 pts (16%). Conversely CRP was raised in 23/32 pts (71.8%). PAP levels were significantly higher in pts with UA than in C (698 ng/ml, range 268-1899 vs 413 ng/ml, range 201-826;  $p = 0.017$ ) but they did not correlate with levels of DD (20.3  $\mu$ g/l, range 5.7-246;  $r = 0.06$ ,  $p = ns$ ) or of TAT (2.1  $\mu$ g/ml, range 0.95-23,  $r = -0.05$ ,  $p = ns$ ). Conversely a significant correlation was observed between PAP and CRP (4.55 mg/l, range 0.7-82;  $r = 0.47$ ,  $p = 0.005$ ). **Conclusions:** In pts with UA there is a

marked activation of plasminogen, with elevation of FAP levels. However this is not associated with activation of hemostasis as detectable by TAT and by elevation of fibrin degradation product as DD, but is associated to elevation of the acute phase protein CRP, suggesting a strong endothelial activation as source of plasminogen production, possibly on an inflammatory basis.

#### 794 Determinants of LV Mass and Wall Motion

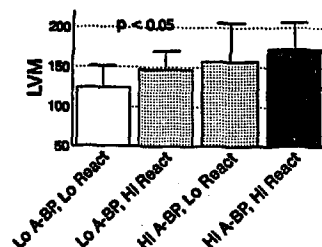
Wednesday, March 27, 1996, 2:00 p.m.—3:30 p.m.  
Orange County Convention Center, Room 222

2:00

#### 794-1 Ambulatory Blood Pressure and Stress Reactivity Predict Left Ventricular Mass

Willem J. Kop, John S. Gottdiener, David S. Krantz. *Uniformed Services Univ of the Health Sciences, Bethesda MD; Georgetown Univ Med Ctr, Washington DC*

Left ventricular mass (LVM) is only moderately correlated with 24-hour ambulatory (A) blood pressure (BP). To determine the contribution of BP reactivity to mental stress (MS), cold pressor (CP) and exercise (EX), 47 healthy subjects (mean age  $35.7 \pm 10.6$ ; 26 women) were studied with math with harassment (MS), and 2 min cold pressor and maximal treadmill EX. LVM on echocardiogram was significantly related to mean A-SBP and A-DBP ( $r = 0.43$  and  $0.35$ , respectively;  $p < 0.05$ ) and LVM was higher among males ( $164.6 \pm 34.0$  vs.  $141.4 \pm 37.2$ ;  $p < 0.04$ ). However, these results were attributable to the association ( $r = 0.60$ ;  $p < 0.001$ ) between LVM and weight. LVM correlated with MS induced SBP increase ( $r = 0.28$ ;  $p < 0.04$ ), which remained significant when baseline hemodynamics (SBP, DBP, and HR), age, gender, weight, and height were controlled for using multiple regression analysis.



Patients with A-SBP above the median ( $> 114$  mmHg) and elevated MS SBP reactivity ( $\Delta$ SBP  $> 17$  mmHg) had the highest LVM. **Conclusion:** Left ventricular mass is increased when both mental stress SBP reactivity and daily life SBP are elevated.

2:15

#### 794-2 Relation of Left Ventricular Contractile Efficiency to Demographic, Metabolic and Anatomic Cardiovascular Risk Factors

Richard B. Devereux, Giovanni de Simone, Thomas G. Pickering, Joseph E. Schwartz, John H. Laragh, Mary J. Roman. *Cornell Medical Center, New York, N.Y.*

Subnormal left ventricular midwall shortening (MWS) in relation to end-systolic LV stress (stress-independent MWS) predicts morbidity and mortality in hypertensive patients with normal LV cavity function. We assessed the relations of LV MW performance to demographic and metabolic variables and to arterial geometry in 303 normals (NL) and 214 hypertensives (HTN) by echocardiography and carotid ultrasound. In multivariate analyses, lower LV MWS and stress-independent MWS in NLS were related to high peripheral resistance, heart rate (both  $p < 0.00001$ ) and cigarette smoking ( $p < 0.05$ ), male gender ( $p < 0.00001$ ), and lower diastolic pressure ( $p < 0.0004$ ) and HDL cholesterol ( $p = 0.003$ ). In HTN, MWS was predicted independently by high resistance ( $p < 0.00001$ ), heart rate ( $p < 0.00005$ ), body mass index ( $p < 0.02$ ) and male gender ( $p < 0.0002$ ) with lesser contributions from age, diastolic pressure and plasma glucose ( $p = 0.01$ – $0.04$ ). In all subjects, low MWS was related to high resistance, heart rate (both  $p < 0.00001$ ) and body mass index ( $p = 0.0003$ ), male gender ( $p < 0.00001$ ) and low age ( $p = 0.001$ ) and diastolic pressure ( $p = 0.002$ ); low stress-independent MWS was predicted by high resistance and heart rate (both  $p < 0.00001$ ), body mass index ( $p = 0.0008$ ), arterial relative wall thickness ( $p < 0.005$ ), cigarette smoking ( $p < 0.01$ ), male gender and lower diastolic pressure (both  $p < 0.00001$ ), age ( $p < 0.00005$ ), arterial expansion in systole ( $p = 0.006$ ) and HDL ( $p = 0.02$ ). Thus,

higher LV contractile function is associated in NL and HTN adults with female gender and more favorable systemic hemodynamics, arterial structure and function, and metabolic variables.

2:30

#### 794-3 Left Ventricular Hypertrophy During Pregnancy — Do Racial Differences Exist?

Patricia Ray, Arthur Pollak, Steven D. Colan, Suzanne M. Mone, Stephen P. Sanders, Rodney H. Falk. *Boston University School of Medicine, Boston, MA; Boston Children's Hospital, Boston, MA*

Left ventricular hypertrophy (LVH) is commoner in Black hypertensive patients than Caucasians matched for resting BP. This suggests a possible racial difference in the LV response to pressure overload. We postulated that if this were true, then differences may occur between Black and Caucasian patients in the physiologic LVH of pregnancy. We studied 33 Caucasian and 17 Black pregnant women during the first trimester and in the peri-partum period. LV mass was calculated from 2-D guided M-mode echo. For the group, LV mass increased by 17% from  $134 \pm 28$  gm to  $157.6 \pm 24$  gm ( $p < 0.01$ ). There were no differences in LV mass or LV mass index between Black and Caucasian patients in the first trimester or in the peripartum period.

	1st Trimester LVM	Peripartum LVM	% Change
Caucasian (n = 33)	$138 \pm 32$ gm	$161 \pm 31$ gm	16.6
Black (n = 17)	$127 \pm 21.4$ gm	$151 \pm 14$ gm	18.8

$p < 0.01$  for 1st trimester/peripartum comparison  $p = NS$  for Caucasian/Black differences.

**Conclusion:** Black and Caucasian women have similar LVH responses to pregnancy. The difference between these findings and the observed racial differences in the LVH response to hypertension may reflect higher peaks of BP during daily activities in hypertensive Blacks and/or a racially different LVH response between the physiologic volume overload of pregnancy and the pathologic pressure overload of hypertension.

2:45

#### 794-4 Elucidation of Regional Heterogeneity in Myocardial Contractile Function With Tagged Cine MRI

Christine H. Lorenz, Jeffrey M. Bundy, John S. Pastorek. *The Jewish Hospital of St. Louis at Washington University Med. Center, St. Louis, MO; Vanderbilt University Med. Center, Nashville, TN*

To define the physiologic pattern of regional intramural contractile function, 10 healthy volunteers (5 F, 5 M, 21–41 y) were studied with tagged cine MRI to assess systolic deformation (strain). Tagged images were acquired at 6 short axis (SA) levels.  $\lambda_1$ , the maximum principal strain, (tissue lengthening) was oriented primarily in the radial direction.  $\lambda_2$ , the minimum principal strain, (shortening) was oriented primarily in the circumferential direction. Strain measurements were performed in 4 cardiac segments (lateral, anterior, septal, and inferior walls) at each SA level (results from 2 of 6 SA levels in table). There was a general trend of decreasing  $\lambda_1$  and increasing  $\lambda_2$  from base to apex.  $\lambda_2$  was significantly different from base to apex only in the septum and inferior wall ( $p < 0.05$ ).  $\lambda_1$  was different from base to apex in all 4 regions ( $p < 0.05$ ). Within each SA slice, strain values were relatively uniform (diff. N.S.) across the 4 wall divisions. These data suggest that shortening is more uniform throughout the heart than is lengthening, and that deformation varies more from base to apex than within any SA slice. Therefore, substantial regional heterogeneity of function is present in normal hearts. Its measurement may permit regional assessment of intramural contractile dysfunction.

		Lateral	Anterior	Septal	Inferior
Base	$\lambda_1$	$0.23 \pm 0.06$	$0.22 \pm 0.05$	$0.23 \pm 0.07$	$0.27 \pm 0.12$
	$\lambda_2$	$-0.31 \pm 0.06$	$-0.31 \pm 0.04$	$-0.28 \pm 0.04$	$-0.29 \pm 0.05$
Apex	$\lambda_1$	$0.16 \pm 0.06$	$0.14 \pm 0.07$	$0.16 \pm 0.07$	$0.15 \pm 0.05$
	$\lambda_2$	$-0.35 \pm 0.04$	$-0.34 \pm 0.04$	$-0.34 \pm 0.06$	$-0.33 \pm 0.06$

3:00

#### 794-5 Characterization of Right Ventricular Contractile Motion With Tagged Cine MRI

Stacy S. Klein, Jeffrey M. Bundy, Christine H. Lorenz. *Vanderbilt University Med. Center, Nashville, TN; The Jewish Hospital of St. Louis at Washington University Med. Center, St. Louis, MO*

Right ventricular myocardial motion has previously been studied with implanted radiopaque markers in animals, but little is known about human RV myocardial motion. Tagged cine MRI was used to define RV motion in 9 normal volunteers (22–30 yrs). The RV was imaged at basal, midventricular,